REMARKS

Applicants thank the Examiner and the Supervisor for the courteous personal interview conducted on April 15, 2003 and for the helpful comments made therein. Presently, Claims 1-8, 18-25 and 34-43 are pending in the application; Claims 9-17 and 26-33 were withdrawn from consideration by the Examiner in the Office Action mailed February 25, 2003. Applicants have now cancelled Claims 1-43, without prejudice, in favor of new Claims 44-74, which are directed to the subject matter of the original Claims 1-8, 18-25 and 34-43 but are presented in a format determined to be allowable at the interview conducted on April 15, 2003. Support for Claims 44-73 can be found throughout the specification and the claims as originally filed with the application (e.g., page 12, lines 21-31; page 30, lines 22-26; page 31, lines 17-31; page 32, lines 1-4; and page 49, lines 1-10).

Information Disclosure Statement

The Examiner notes that reference 21 of the Information Disclosure Statement filed on August 27, 2002 included only pages 1 and 2. A complete submission was filed in an Information Disclosure Statement on May 6, 2003. With respect to reference 19 of the Information Disclosure Statement filed on August 27, 2002, Applicants do not have a translation of this reference and appreciate that the reference has only been considered to the extent of the contents of the Abstract in the English language.

Drawings

The Examiner has indicated that formal drawings are required in this application. Applicants submit herewith an amendment to enter the formal drawings attached hereto into the present application.

Priority

Applicants thank the Examiner for acknowledging the claimed foreign priority based on an application filed in Sweden on November 24, 1998. Applicants file herewith a certified copy of said priority document, which was filed in English.

Specification

The Examiner has objected to the consistency of Figures 8A-H with their description and the relevant pages of the specification. Applicants have amended Figure 8 and the specification so that the description of the subject matter uses the same numeric identification. No new matter has been introduced by these amendments.

Rejections under 35 U.S.C. § 112, ¶ 2

The Examiner has rejected the claims for using the term "cell growth," which, according to the Examiner, does not clearly define the claims as to whether the inhibition of cell growth is due to an inhibition of the increase in size or maturity of cells. The Examiner has also indicated that it is not clear what is meant by the term "parvovirus VP2 capsid." The Examiner also argues that it is not clear as to why the step of "measuring the inhibition of growth of said hematopoietic cells" is present in some of the claims and, further, the Examiner argues that Claims 7 and 8 do not make it clear as to what the reduction in hematocrit or hematopoietic cells is in reference to.

Claims 37 and 42 have also been rejected under 35 U.S.C. § 112 because they refer to a SEQ ID NO that provides a sequence that does not comprise the sequence QQY.

Applicants respectfully submit that the amendments overcome the aforementioned rejections. Specifically, the claims now refer to an "inhibition of hematopoiesis," instead of "cell growth" and "VP2 protein" instead of "parvovirus VP2 capsid." These amendments were agreed to be acceptable at the interview of April 15, 2003. Also discussed and agreed at the interview of April 15, 2003 was that the step of "measuring the inhibition of growth of said hematopoietic cells" was acceptable.

The rejections of Claims 7, 8, 37 and 42 under 35 U.S.C. § 112, ¶ 2, have been obviated by amendment and Applicants respectfully submit that all of the rejections under 35 U.S.C. § 112, ¶ 2 have been overcome.

Rejections under 35 U.S.C. § 112, ¶ 1

The Examiner rejects Claims 1, 2, 4, 7, 8, 18, 19, 21, 24 and 25 under 35 U.S.C. § 112, ¶ 1, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors at the time the application was filed had possession of the claimed invention. The Examiner argues that the specification does not provide sufficient written description support for a claim to a genus of trimer peptides with the claimed function. The Examiner refers to *Eli Lilly*, 119 F.3d at 1568, 43 U.S.P.Q.2d at 1406, for the proposition that Applicants are required to describe a sufficient variety of species of trimers that inhibit hematopoiesis in order to meet the written description requirements of a genus claim. Although the Examiner recognizes that Applicants have disclosed a VP2 trimer that is effective at inhibiting the growth of hematopoietic cells and several other fragments of VP2 that inhibit the growth of hematopoietic cells, the Examiner continues to argue that the specification does not provide written description support for any VP2 trimer capable of inhibiting hematopoietic cell growth.

Although Applicants have amended the claims to traverse the written description rejections above, Applicants reserve the right to prosecute any omitted subject matter in a continuation application.

Applicants also respectfully submit that the Examiner's interpretation of the requirements under 35 U.S.C. § 112, ¶ 1, do not reflect the current status of the law of written description, as set forth by the Federal Circuit in *Moba v. Diamond Automation,* decided April 1, 2003. In *Moba,* the Federal Circuit confirmed the rule set forth in *EnzoBiochem, Inc. v. Gen-probe, Inc.* 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002), which distinguished the holding of *Eli Lilly.* In discussing the written description test, the Federal Circuit reiterates the instructions given in *Enzo*:

> On remand the court should determine whether a person of skill in the art would glean from the written description, including information obtainable from the deposits of the claimed sequences, subsequences, mutated variants and mixtures sufficient to demonstrate possession of the generic scope of the claims. *Enzo*, 296

F.3d at 1328

and that

> More recently, in Enzo Biochem, we clarified that Eli Lilly did not hold that all functional descriptions of genetic material necessarily fail as a matter of law to meet the written description requirement; rather, the requirement may be satisfied if in the knowledge of the art the disclosed function is sufficiently correlated to a particular, known structure. Amgen Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1332, 65 USPQ2d 1385 (Fed. Cir. 2003).

In addition to showing that the full-length VP2 protein inhibits hematopoiesis, Applicants have shown that fragments of VP2 protein as small as 3, 4, 6, 8, 10, 12, 16, 20, and 21 amino acids are of a length sufficient to inhibit hematopoiesis (*See e.g., Tables 6 and 7*). Applicants have also shown that enzymatically cleaved fragments of VP2 protein (LYS-C endoprotease and ARG-C endoprotease) are of a length sufficient to inhibit hematopoiesis. (*See Figures 7A-C).* Thus, the disclosed function (inhibition of hematopoiesis) is, in fact, associated with the structure (multiple fragments of VP2 protein of various lengths). Applicants have also shown that fragments all along the entire length of the VP2 protein inhibit hematopoiesis and that the QQY motif, which appears only once in the VP2 molecule, is not a required element for a fragment to inhibit hematopoiesis. (*See Table 6, pools 1, 2, 3, 4, 5, 7, and 8).* Thus, it is clear to one of skill in the art that fragments of various lengths throughout the VP2 protein inhibit hematopoiesis.

The written description requirement is not a "Super Enablement" requirement and Applicants are not required to describe exactly the subject matter claimed to demonstrate possession of the invention. *See Moba* supra. Applicants have provided numerous working examples of fragments of VP2 protein that are of a length sufficient to inhibit hematopoiesis. Applicants respectfully submit that they have meet the written description requirement set forth by 35 USC §112, as interpreted by the Federal Circuit, and request that these rejections be withdrawn.

The Examiner has also rejected the claims under 35 U.S.C.§112, paragraph 1, for lack of enablement. The Examiner states that the enablement rejection has two parts: (1) the specification does not enable the use of any fragment of the VP2 capsid that is at least three amino acids in length and (2) that the specification does not enable the use of peptides *in vivo.* During the interview of April 15, 2003, Applicants presented an exhibit, which showed that VP2 protein effectively inhibited hematopoiesis in monkeys. Although the Examiner was willing to remove the enablement rejection with respect to methods of inhibiting hematopoiesis in healthy subjects, the Examiner indicated that more was needed to enable claims directed to the treatment of subjects in need or subjects afflicted with hyperproliferative disorders. The Examiner stated that he was open to more information by way of declaration, however, in particular a third party declaration that indicates that one of skill in the art would appreciate that the identified peptides would be likely useful or accepted for therapeutic application.

Although Applicants submit that they have enabled the use of fragments of VP2 protein

comprising at least three consecutive amino acids of VP2 protein, Applicants have amended the claims to traverse the first part of the enablement rejection. Applicants reserve the right to pursue claims directed to any omitted subject matter in a continuation application.

As stated above, Applicants have shown that fragments of VP2 protein as small as 3, 4, 6, 8, 10, 12, 16, 20, and 21 amino acids are of a length sufficient to inhibit hematopoiesis (*See e.g., Tables 6 and 7*). Applicants have also shown that enzymatically cleaved fragments of VP2 protein (LYS-C endoprotease and ARG-C endoprotease) are of a length sufficient to inhibit hematopoiesis. (*See Figures 7A-C)*. Applicants have also shown that fragments all along the entire length of the VP2 protein inhibit hematopoiesis and that the QQY motif, which appears only once in the VP2 molecule, is not a required element for a fragment to inhibit hematopoiesis. (*See Table 6, pools 1, 2, 3, 4, 5, 7, and 8)*. Thus, it is clear to one of skill in the art that fragments of various lengths throughout the VP2 protein inhibit hematopoiesis. At a minimum, undue experimentation is not required for the skilled artisan to practice the full scope of the invention. Several working examples of fragments of VP2 protein of sufficient length to inhibit hematopoiesis have been provided and their use in inhibiting hematopoiesis has been shown. Although a working example of every possible fragment of VP2 protein of sufficient length to inhibit hematopoiesis has not been provided, this is not required under the law. Applicants respectfully submit that they have overcome the rejections for lack of enablement as set forth in the first part of the enablement rejection.

Applicants also provide a declaration from Anders Vahlne Ph.D., M.D, which states that it is his opinion that the application and the appended data (Exhibits A and B) show that VP2 protein and fragments of VP2 protein of varying lengths, corresponding to various regions of the VP2 molecule, inhibit hematopoiesis. Dr. Vahlne also states that the data provide strong evidence that VP2 protein can be used to treat hematological proliferative disorders such as Polycythemia Vera, as well as, inhibit hematopoiesis in healthy subjects. Lastly, Dr. Vahlne states that the data in the specification strongly supports a finding that fragments of VP2 protein of sufficient length to inhibit hematopoiesis are therapeutically efficacious. Applicants respectfully submit that they have overcome the rejections under 35 U.S.C. § 112, ¶ 1 and request that the Examiner withdraw these rejections.

CONCLUSION

Based on the foregoing, Applicants respectfully submit that the application is now in condition for allowance and such action is earnestly solicited. The undersigned has made a good faith effort to respond to all of the rejections in the case and to place the claims in condition for immediate allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is respectfully requested to call Applicant's attorney, Eric S. Furman at (619) 687-8643 (direct line), to resolve such issue promptly.

This response has been filed with a three-month extension fee. No further fees are seen as being necessary. However, the Commissioner is authorized to charge any fees in connection with this paper to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 8/12/03

By: _____

Eric S. Furman, Ph.D.
Registration No. 45,664
Attorney of Record
Customer No. 20,995
(619) 235-8550

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EXHIBIT A

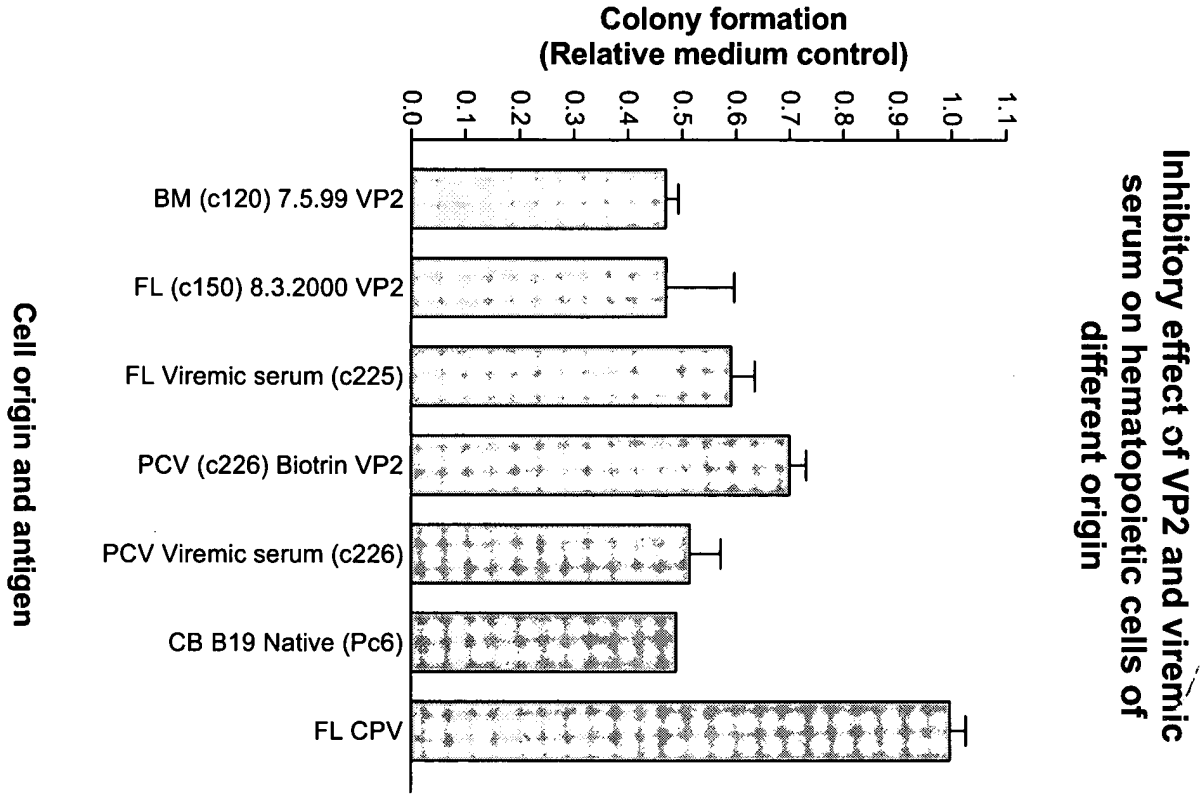

EXHIBIT B